

What is claimed is:

1. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence homologous to a sequence selected from the group consisting of: SEQ ID NO:2 and SEQ ID NO:4, and fragments thereof; said nucleic acid molecule encoding at least a portion of Con-218.
2. The isolated nucleic acid molecule of claim 1 comprising a sequence that encodes a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4, and fragments thereof.
3. The isolated nucleic acid molecule of claim 1 comprising a sequence homologous to a sequence of SEQ ID NO:1 or SEQ ID NO:3, and fragments thereof.
4. The isolated nucleic acid molecule of claim 1 comprising a sequence of SEQ ID NO:1 or SEQ ID NO:3, and fragments thereof.
5. The isolated nucleic acid molecule of claim 1 wherein said nucleic acid molecule is DNA.
6. The isolated nucleic acid molecule of claim 1 wherein said nucleic acid molecule is RNA.
7. An expression vector comprising a nucleic acid molecule of any one of claims 1 to 4.

8. The expression vector of claim 7 wherein said nucleic acid molecule comprises a sequence of SEQ ID NO:1 or SEQ ID NO:3.
9. The expression vector of claim 7 wherein said vector is a plasmid.
10. The expression vector of claim 7 wherein said vector is a viral particle.
11. The expression vector of claim 10 wherein said vector is selected from the group consisting of adenoviruses, baculoviruses, parvoviruses, herpesviruses, poxviruses, adeno-associated viruses, Semliki Forest viruses, vaccinia viruses, and retroviruses.
12. The expression vector of claim 7 wherein said nucleic acid molecule is operably connected to a promoter selected from the group consisting of simian virus 40, mouse mammary tumor virus, long terminal repeat of human immunodeficiency virus, maloney virus, cytomegalovirus immediate early promoter, Epstein Barr virus, rous sarcoma virus, human actin, human myosin, human hemoglobin, human muscle creatine, and human metallothionein.
13. A host cell transformed with an expression vector of claim 7.
14. The transformed host cell of claim 13 wherein said cell is a bacterial cell.
15. The transformed host cell of claim 14 wherein said bacterial cell is E. coli.
16. The transformed host cell of claim 13 wherein said cell is yeast.
17. The transformed host cell of claim 16 wherein said yeast is S. cerevisiae.

18. The transformed host cell of claim 13 wherein said cell is an insect cell.
19. The transformed host cell of claim 18 wherein said insect cell is *S. frugiperda*.
20. The transformed host cell of claim 13 wherein said cell is a mammalian cell.
21. The transformed host cell of claim 20 wherein mammalian cell is selected from the group consisting of chinese hamster ovary cells, HeLa cells, African green monkey kidney cells, human 293 cells, and murine 3T3 fibroblasts.
22. An isolated nucleic acid molecule comprising a nucleotide sequence complementary to at least a portion of SEQ ID NO:1 or SEQ ID NO:3, said portion comprising at least 10 nucleotides.
23. The nucleic acid molecule of claim 22 wherein said molecule is an antisense oligonucleotide directed to a region of SEQ ID NO:1 or SEQ ID NO:3.
24. The nucleic acid molecule of claim 23 wherein said oligonucleotide is directed to a regulatory region of SEQ ID NO:1 or SEQ ID NO:3.
25. A composition comprising a nucleic acid molecule of any one of claims 1 to 4 or 27 and an acceptable carrier or diluent.
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26. A composition comprising a recombinant expression vector of claim 7 and an acceptable carrier or diluent.

27. A method of producing a polypeptide that comprises a sequence selected from the group sequences consisting SEQ ID NO:2 and SEQ ID NO:4, and homologs and fragments thereof, said method comprising the steps of:

- a) introducing a recombinant expression vector of claim 7 into a compatible host cell;
- b) growing said host cell under conditions for expression of said polypeptide; and
- c) recovering said polypeptide.

28. The method of claim 27 wherein said host cell is lysed and said polypeptide is recovered from the lysate of said host cell.

29. The method of claim 27 wherein said polypeptide is recovered by purifying the culture medium without lysing said host cell.

30. An isolated polypeptide ~~encoded by a nucleic acid molecule~~ of claim 1.

31. The polypeptide of claim 30 wherein said polypeptide comprises a sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4.

32. The polypeptide of claim 30 wherein ~~said~~ polypeptide comprises an amino acid sequence homologous to a sequence ~~selected from the group consisting of~~ SEQ ID NO:2 and SEQ ID NO:4.

33. The polypeptide of claim 30 wherein ~~said~~ sequence homologous to a sequence selected from the group consisting of ~~SEQ ID NO:2 and SEQ ID NO:4~~ comprises at least one

conservative amino acid substitution compared to the even numbered sequences in the group consisting of SEQ ID NO:2 and SEQ ID NO:4.

34. The polypeptide of claim 30 wherein said polypeptide comprises a fragment of a polypeptide with a sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4.

35. A composition comprising a polypeptide of claim 30 and an acceptable carrier or diluent.

36. An isolated antibody which binds to an epitope on a polypeptide of claim 30.

37. The antibody of claim 36 wherein said antibody is a monoclonal antibody.

38. A composition comprising an antibody of claim 36 and an acceptable carrier or diluent.

39. A method of inducing an immune response in a mammal against a polypeptide of claim 30 comprising administering to said mammal an amount of said polypeptide sufficient to induce said immune response.

40. A method for identifying a compound which binds Con-218 comprising the steps of:

a) contacting Con-218 with a compound; and
determining whether said compound binds Con-218.

41. The method of claim 40 wherein the Con-218 comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4.

42. The method of claim 40 wherein binding of said compound to Con-218 is determined by a protein binding assay.

43. The method of claim 40 wherein said protein binding assay is selected from the group consisting of a gel-shift assay, Western blot, radiolabeled competition assay, phage-based expression cloning, co-fractionation by chromatography, co-precipitation, cross linking, interaction trap/two-hybrid analysis, southwestern analysis, and ELISA.

44. A compound identified by the method of claim 40.

45. A method for identifying a compound which binds a nucleic acid molecule encoding Con-218 comprising the steps of:

- a) contacting said nucleic acid molecule encoding Con-218 with a compound; and
- b) determining whether said compound binds said nucleic acid molecule.

46. The method of claim 45 wherein binding is determined by a gel-shift assay.

47. A compound identified by the method of claim 45.

48. A method for identifying a compound which modulates the activity of Con-218 comprising the steps of:

- a) contacting Con-218 with a compound; and
- b) determining whether Con-218 activity has been modulated.

49. The method of claim 48 wherein the Con-218 comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4.

50. The method of claim 48 wherein said activity is neuropeptide binding.

51. The method of claim 48 wherein said activity is neuropeptide signaling.

52. A compound identified by the method of claim 48.

53. A method of identifying an animal homolog of Con-218 comprising the steps:
a) comparing the nucleic acid sequences of the animal with a sequence of SEQ ID NO:1, and portions thereof, said portions being at least 10 nucleotides; and
b) identifying nucleic acid sequences of the animal that are homologous to said sequence of SEQ ID NO: 1 or 3, and portions thereof.

54. The method of claim 53 wherein comparing the nucleic acid sequences of the animal with a sequence of SEQ ID NO:1 or SEQ ID NO:3, and portions thereof, said portions being at least 10 nucleotides, is performed by DNA hybridization.

55. The method of claim 53 wherein comparing the nucleic acid sequences of the animal with a sequence of SEQ ID NO:1 or SEQ ID NO:3, and portions thereof, said portions being at least 10 nucleotides, is performed by computer homology search.

56. A method of screening a human subject to diagnose a disorder affecting the brain or genetic predisposition therefor, comprising the steps of:

(a) assaying nucleic acid of a human subject to determine a presence or an absence of a mutation altering an amino acid sequence, expression, or biological activity of Con-218, wherein Con-218 comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:2 and SEQ ID NO:4, and allelic variants thereof, and wherein the nucleic acid corresponds to a gene encoding Con-218; and

(b) diagnosing the disorder or predisposition from the presence or absence of said mutation, wherein the presence of a mutation altering the amino acid sequence, expression, or biological activity of Con-218 correlates with an increased risk of developing the disorder.

57. A method according to claim 56, wherein the disease is schizophrenia.

58. A method according to claim 56, wherein the assaying step comprises at least one procedure selected from the group consisting of:

a) comparing nucleotide sequences from the human subject and reference sequences and determining a difference of either

at least a nucleotide of at least one codon between the nucleotide sequences from the human subject that encodes an Con-218 allele and an Con-218 reference sequence, or

(b) performing a hybridization assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences;

(c) performing a polynucleotide migration assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences; and

(d) performing a restriction endonuclease digestion to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences.

59. A method according to claim 58 wherein the assaying step comprises: performing a polymerase chain reaction assay to amplify nucleic acid comprising Con-218 coding sequence, and determining nucleotide sequence of the amplified nucleic acid.

60. A method of screening for an Con-218 hereditary schizophrenia genotype in a human patient, comprising the steps of:

- (a) providing a biological sample comprising nucleic acid from said patient, said nucleic acid including sequences corresponding to alleles of Con-218; and
- (b) detecting the presence of one or more mutations in the Con-218 allele;

wherein the presence of a mutation in an Con-218 allele is indicative of a hereditary schizophrenia genotype.

61. The method according to claim 60 wherein said biological sample is a cell sample.

62. The method according to claim 60 wherein said detecting the presence of a mutation comprises sequencing at least a portion of said nucleic acid, said portion comprising at least one codon of said Con-218 allele.

63. The method according to claim 60 wherein said nucleic acid is DNA.

64. The method according to claim 60 wherein said nucleic acid is RNA.

65. A kit for screening a human subject to diagnose schizophrenia or a genetic predisposition therefor, comprising, in association:

(a) an oligonucleotide useful as a probe for identifying polymorphisms in a human Con-218 gene, the oligonucleotide comprising 6-50 nucleotides in a sequence that is identical or complementary to a sequence of a wild type human Con-218 gene sequence or Con-218 coding sequence, except for one sequence difference selected from the group consisting of a nucleotide addition, a nucleotide deletion, or nucleotide substitution; and

(b) a media packaged with the oligonucleotide, said media containing information for identifying polymorphisms that correlate with schizophrenia or a genetic predisposition therefor, the polymorphisms being identifiable using the oligonucleotide as a probe.

66. A method of identifying a nGPCR allelic variant that correlates with a mental disorder, comprising steps of:

(a) providing a biological sample comprising nucleic acid from a human patient diagnosed with a mental disorder, or from the patient's genetic progenitors or progeny;

(b) detecting in the nucleic acid the presence of one or more mutations in Con-218, wherein Con-218 comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4, and allelic variants thereof, and wherein the nucleic acid includes sequence corresponding to the gene or genes encoding Con-218;

wherein the one or more mutations detected indicates an allelic variant that correlates with a mental disorder.

67. A method according to claim 66, wherein the disorder is schizophrenia.

68. A purified and isolated polynucleotide comprising a nucleotide sequence encoding a Con-218 allelic variant identified according to claim 67.

69. A host cell transformed or transfected with a polynucleotide according to claim 68 or with a vector comprising the polynucleotide.

70. A purified polynucleotide comprising a nucleotide sequence encoding Con-218 of a human with schizophrenia;

wherein said polynucleotide hybridizes to the complement of SEQ ID NO:1 or SEQ ID NO:3 under the following hybridization conditions:

(a) hybridization for 16 hours at 42°C in a hybridization solution comprising 50% formamide, 1% SDS, 1 M NaCl, 10% dextran sulfate and

(b) washing 2 times for 30 minutes at 60°C in a wash solution comprising 0.1x SSC and 1% SDS; and

wherein the polynucleotide that encodes Con-218 amino acid sequence of the human differs from SEQ ID NO:2 or SEQ ID NO:4 by at least one residue.

71. A vector comprising a polynucleotide according to claim 70.

72. A host cell that has been transformed or transfected with a polynucleotide according to claim 70 and that expresses the Con-218 protein encoded by the polynucleotide.

73. A host cell according to claim 72 that has been co-transfected with a polynucleotide encoding the Con-218 amino acid sequence set forth in SEQ ID NO:2 or SEQ ID NO:4 and that expresses the Con-218 protein having the amino acid sequence set forth in SEQ ID NO:2 or SEQ ID NO:4.

74. A method for identifying a modulator of biological activity of Con-218 comprising the steps of:

a) contacting a cell according to claim 72 in the presence and in the absence of a putative modulator compound;

b) measuring Con-218 biological activity in the cell;

wherein decreased or increased Con-218 biological activity in the presence versus absence of the putative modulator is indicative of a modulator of biological activity.

75. A method to identify compounds useful for the treatment of schizophrenia, said method comprising steps of:

(a) contacting a composition comprising Con-218 with a compound suspected of binding Con-218;

(b) detecting binding between Con-218 and the compound suspected of binding Con-218;

wherein compounds identified as binding Con-218 are candidate compounds useful for the treatment of schizophrenia.

76. A method for identifying a compound useful as a modulator of binding between Con-218 and a binding partner of Con-218 comprising the steps of:

(a) contacting the binding partner and a composition comprising Con-218 in the presence and in the absence of a putative modulator compound;

(b) detecting binding between the binding partner and Con-218;

wherein decreased or increased binding between the binding partner and Con-218 in the presence of the putative modulator, as compared to binding in the absence of the putative modulator is indicative a modulator compound useful for the treatment of schizophrenia.

77. A method according to claim 75 or 76 wherein the composition comprises a cell expressing Con-218 on its surface.

78. A method according to claim 77 wherein the composition comprises a cell transformed or transfected with a polynucleotide that encodes Con-218.

79. A method of purifying a G protein from a sample containing said G protein comprising the steps of:

- a) contacting said sample with a polypeptide of claim 1 for a time sufficient to allow said G protein to form a complex with said polypeptide;
- b) isolating said complex from remaining components of said sample;
- c) maintaining said complex under conditions which result in dissociation of said G protein from said polypeptide; and
- d) isolating said G protein from said polypeptide.

80. The method of claim 79 wherein said sample comprises an amino acid sequence selected from the group of sequences consisting of SEQ ID NO:2 and SEQ ID NO:4.

81. The method of claim 79 wherein said polypeptide comprises an amino acid sequence homologous to a sequence selected from the group of sequences consisting of SEQ ID NO:2 and SEQ ID NO:4.